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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,883	08/25/2005	Jorg Peters	Le A 36 075	7044
35969 7590 03/05/2008 Bayer Health Care LLC 400 Morgan Lane West Haven, CT 06516				
EXAMINER				
LI, RUIXIANG				
ART UNIT		PAPER NUMBER		
1646				
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03/05/2008		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/520,883

**Applicant(s)**

PETERS ET AL.

**Examiner**

RUIXIANG LI

**Art Unit**

1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SF 298)  
Paper No(s)/Mail Date 01/10/2005
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_

## **DETAILED ACTION**

### ***Status of Application, Amendments, and/or Claims***

1. Applicants' preliminary amendment filed on 01/10/2005 has been entered in full.  
Claims 1-10 are pending and under consideration.

### ***Information Disclosure Statement***

2. The information disclosure statement filed on 01/10/2005 is considered by the Examiner and a signed copy has been attached to the office action.

### ***Claim Rejections—35 U.S.C. §102 (b)***

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-6 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Domingues et al. (Journal of Biotechnology 84:217-230, 2000).

Domingues et al. teach a method for preparation of interleukin-4 or mutants by recombinant expression comprising (a) expression in inclusion bodies (page 220, right column, the 3<sup>rd</sup> paragraph), (b) disrupting the cells and separating the inclusion bodies, (c) washing inclusion bodies obtained with 0.1 M Tris-HCl pH8/1 mM EDTA/0.1% zwittergent, (d) solubilizing the inclusion bodies by denaturation, (e)

renaturing the expression product and purifying the expression product by cross-flow ultrafiltration against five volumes of buffer (page 220, right column, the 4th paragraph to page 221, the first paragraph of left column). Thus, the reference of Domingues et al. meets the limitations of claims 1-6 and 8.

5. Claims 1, 4-6, 8, and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Kastelein et al. (EP 0301835 A1, February 1, 1989).

Kastelein et al. teach a method for refolding and purifying interleukin-4 expressed in *Escherichia* cells (page 2, lines 20-41; claim 1; Examples 1-2) comprising (a) expression in inclusion bodies, (b) disrupting the cells and separating the inclusion bodies, (c) washing inclusion bodies obtained with buffer solution (page 4, lines 20-22), (d) solubilizing the inclusion bodies by denaturation, (e) renaturing the expression product by dialysis (page 6, lines 50-59; page 8, lines 61-63) and purifying the expression product by gel filtration chromatography (claim 9). Kastelein et al. further teach the buffer solution comprises 50 mM Tris, 50 mM NaCl, 1 mM EDTA, 0.1 mM PMSF, pH8.0) (page 8, lines 35-38, 51-52). Thus, the reference of Kastelein et al. meets the limitations of claims 1, 4-6, 8, and 10.

***Claim Rejections Under 35 U.S.C. §103 (a)***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Domingues et al. (Journal of Biotechnology 84:217-230, 2000), as applied to claims 1-6 and 8 above, and further in view of Apeler et al. (EP 1022337 A2, 07/26/2000).

Domingues et al. teach a method for preparation of interleukin-4 or mutants by recombinant expression as applied to claims 1-6 and 8 above.

Domingues et al. fail to teach a method for preparation of an interleukin-4 mutant, Interleukin-4 R121D Y124D, by recombinant expression.

Apeler et al. teach expression of a human interleukin-4 mutant, Interleukin-4 R121D Y124D (page 2, paragraphs [0002] and [0007]).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Domingues et al. to prepare interleukin-4 R121D Y124D with a reasonable expectation of success. One would have been motivated to do so because the method of Domingues et al. has been shown to be successful in preparation of interleukin-4 mutants (see, e.g., Table 2), whereas interleukin-4 R121D Y124D is able to block both IL-4 and IL-13 activities and may be useful as a therapeutic agent as taught by Apeler et al. (page 2, paragraphs [0003]).

8. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Domingues et al. (Journal of Biotechnology 84:217-230, 2000), as applied to claims 1-6 and 8 above, and further in view of Gellman et al. (US Patent No. 5,563,057, October 8, 1996).

Domingues et al. teach a method for preparation of interleukin-4 or mutants by recombinant expression as applied to claims 1-6 and 8 above.

Domingues et al. fail to teach the renaturation of interleukin-4 or mutants by dialysis in the presence of artificial chaperones.

Gellman et al. teach the use of artificial chaperones, such as  $\beta$ -cyclodextrin for refolding enzymes (see Example 1).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Domingues et al. to use artificial chaperones, such as  $\beta$ -cyclodextrin for refolding interleukin-4 or mutants with a reasonable expectation of success. One would have been motivated to do so because artificial chaperones, such as  $\beta$ -cyclodextrin, cause the detergents to be sequestered from a protein and detergent complex and allow the protein to achieve the correct folding as demonstrated by Gellman et al. (see, e.g., Example 1).

***Claim Objections—Minor Informality***

9. Claim 9 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 9 recites a limitation, "wherein the renaturation (e) is done in the presence of artificial chaperones". However, claim 8 already has the limitation, "optionally in the presence of artificial chaperones".

***Conclusion***

10. No claims are allowed.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status

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information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

/Ruixiang Li/

Primary Examiner, Art Unit 1646

Ruixiang Li, Ph.D.

February 26, 2008